



## Analysis of dDNP NMR metabolic data from cancer cells (- poster)

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*Publication date:*  
2018

*Document Version*  
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

*Citation (APA):*  
Frahm, A. B., Lundsgaard, E. A., Matei, A., Jensen, P. R., Karlsson, M., Ardenkjær-Larsen, J. H., & Lerche, M. H. (2018). *Analysis of dDNP NMR metabolic data from cancer cells (- poster)*. Poster session presented at International Conference on Nuclear Hyperpolarization 2018, Southampton , United Kingdom.

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# Analysis of dDNP NMR metabolic data from cancer cells



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## Prostate cancer

To prevent unnecessary and expensive treatment of benign prostate cancer, more sensitive tools are needed. Metabolomics combined with datamining have shown great potential for locating motifs and biomarkers for prostate cancer. [1]  
The aim of this project is to use metabolic data to distinguish between aggressive and benign prostate cancer cell lines. Four cell lines are analysed: PC3 and DU145 (aggressive), and Ln-Cap and PNT1a (non-aggressive).

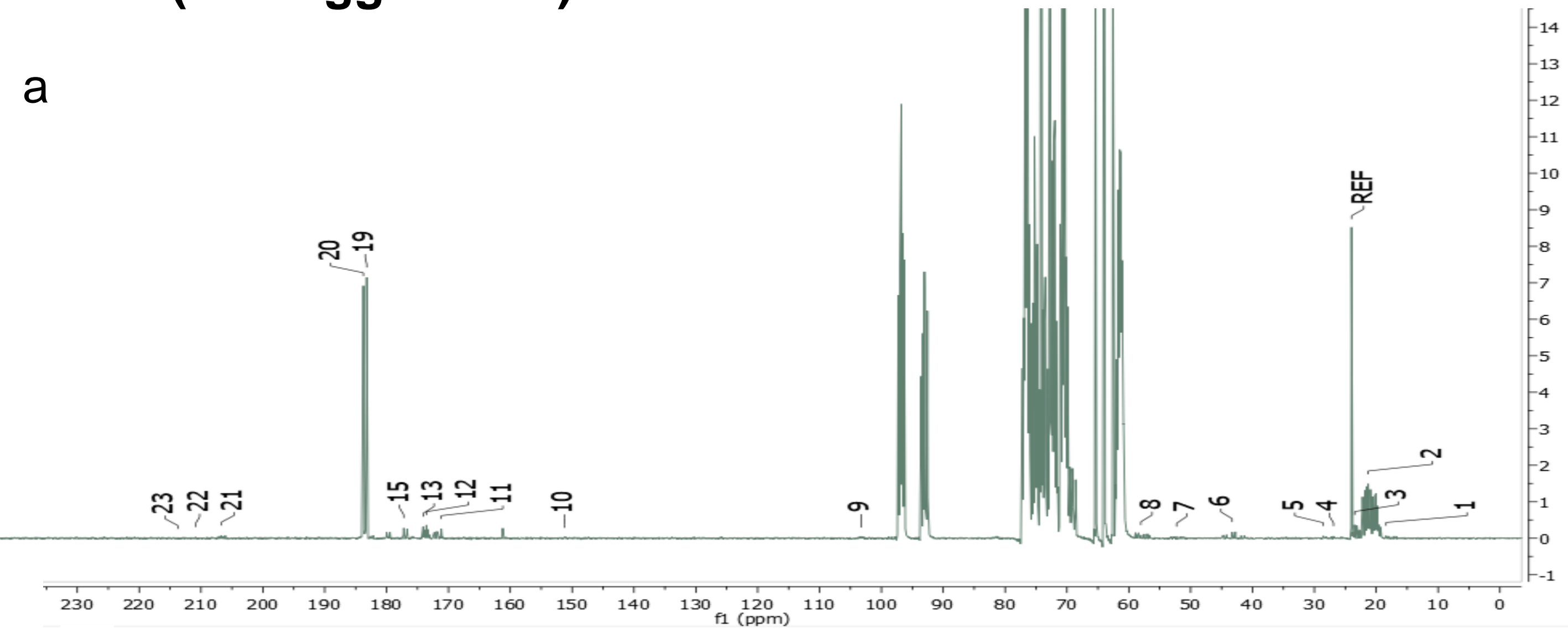
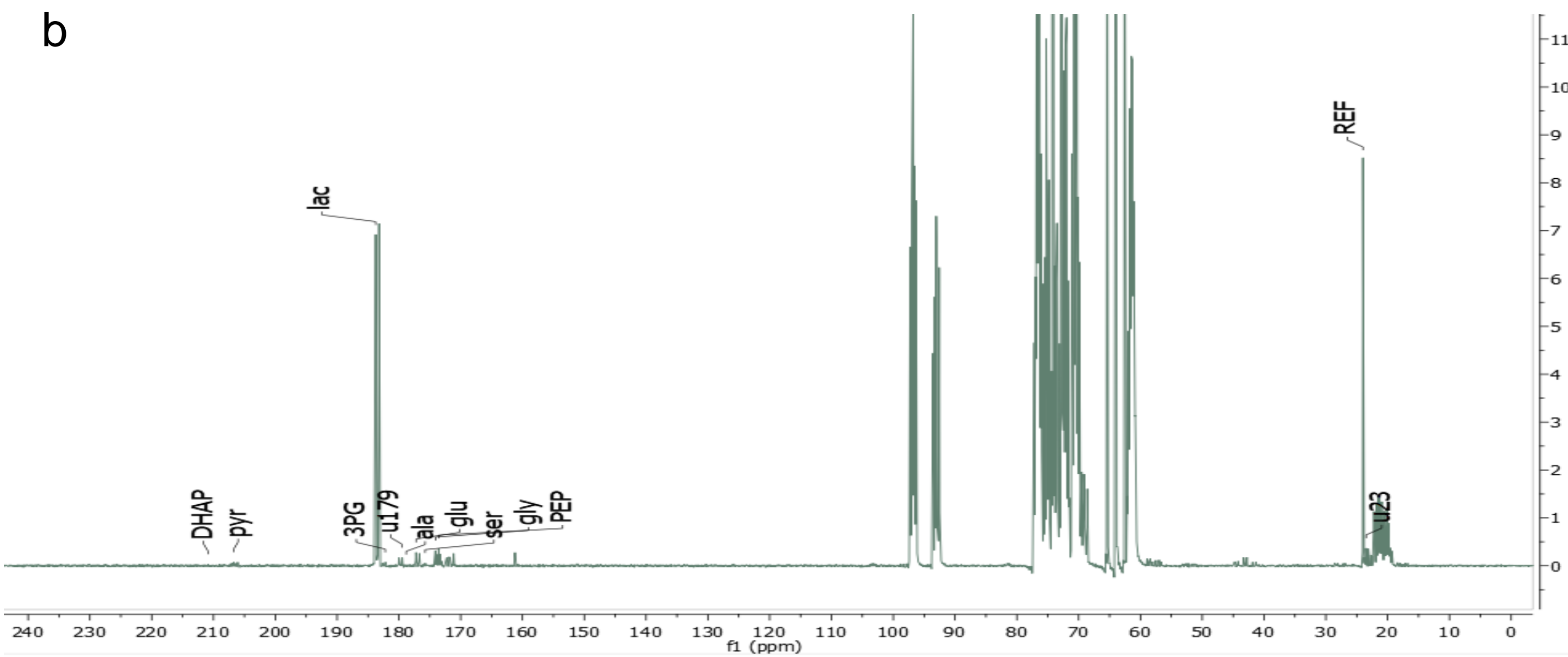


Figure 1: Spectrum from [cell line] cells. Peaks measured for peak data (a) and met. Data (b)

## Metabolic fingerprint

Cells were incubated for 30 minutes with <sup>13</sup>C6-d7 isotope labeled glucose, before metabolites were harvested and hyperpolarized with dissolution Dynamic Nuclear Polarization (dDNP). This technique has been shown to be quantitative and reproducible. [2] From the resulting spectra, integrals of peaks were measured and two dataset were generated. One with standardized peak values for each peak outside the glucose area (peak data) and one where these peaks were collected to metabolites (met. data).



## PC-DFA results

Results from Principal Component-Discriminant Function Analysis (PC-DFA) are shown in fig.2 and summarized in table 1. With leave-One-Out cross-validation classification of aggressive v. non-aggressive is 96.6% correct for peak data and 93.1% for met. data.

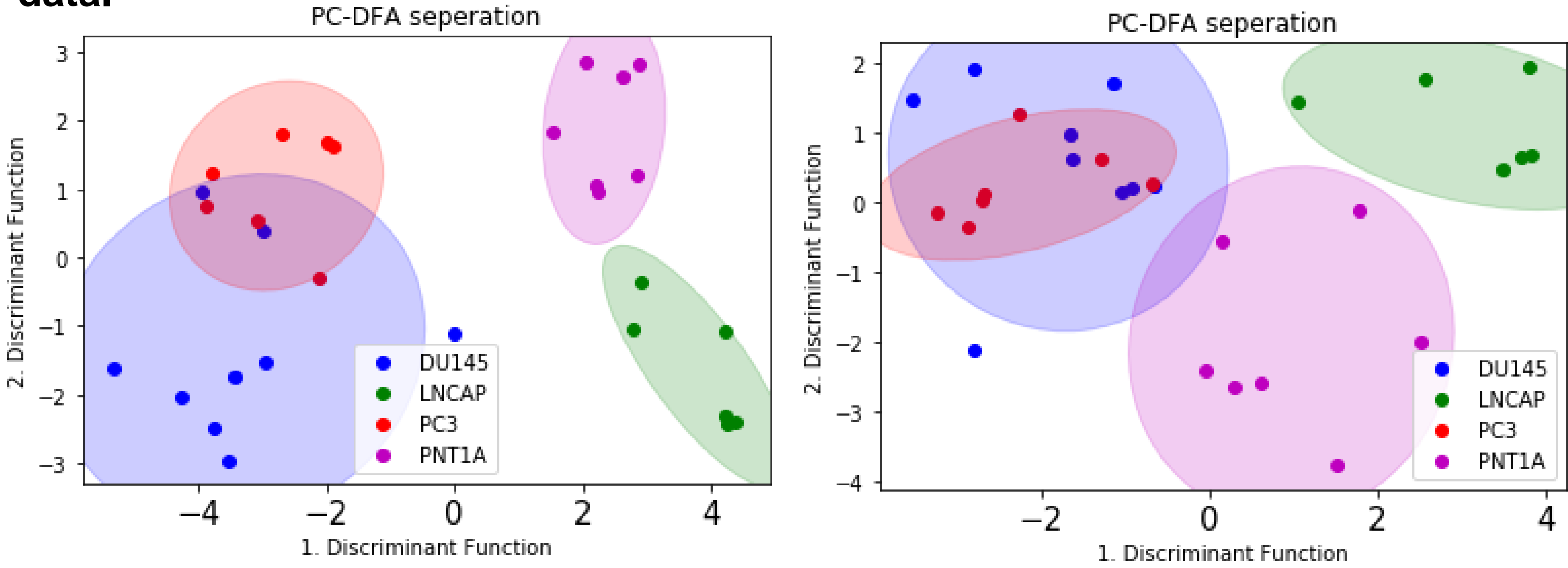


Figure 2: PC-DFA model for peak data (left) and met. data (right). Discriminant function axes are made to optimize distance between classes. Circles mark 2 standard deviations.

Peak data					Met. Data						
No validation		Predicted class				No validation		Predicted class			
		DU145	PC3	Ln-CAP	PNT1a			DU145	PC3	Ln-CAP	PNT1a
True class	DU145	8	1	0	0	True class	DU145	8	1	0	0
	PC3	0	7	0	0		PC3	0	7	0	0
	Ln-CAP	0	0	6	0		Ln-CAP	0	0	6	0
	PNT1a	0	0	0	7		PNT1a	0	0	1	6
Cross-Validation		Predicted class				Cross-Validation		Predicted class			
		DU145	PC3	Ln-CAP	PNT1a			DU145	PC3	Ln-CAP	PNT1a
True class	DU145	4	4	0	1	True class	DU145	4	5	0	0
	PC3	2	5	0	0		PC3	3	4	0	0
	Ln-CAP	0	0	5	1		Ln-CAP	0	1	4	1
	PNT1a	0	0	2	5		PNT1a	1	0	1	5

Table 1: Results of PC-DFA classification.

## Random Forest Feature Extraction

Random Forest (RF) analysis was used to examine what features are important for differentiating between the cell lines. Results are shown in fig. 3 below.

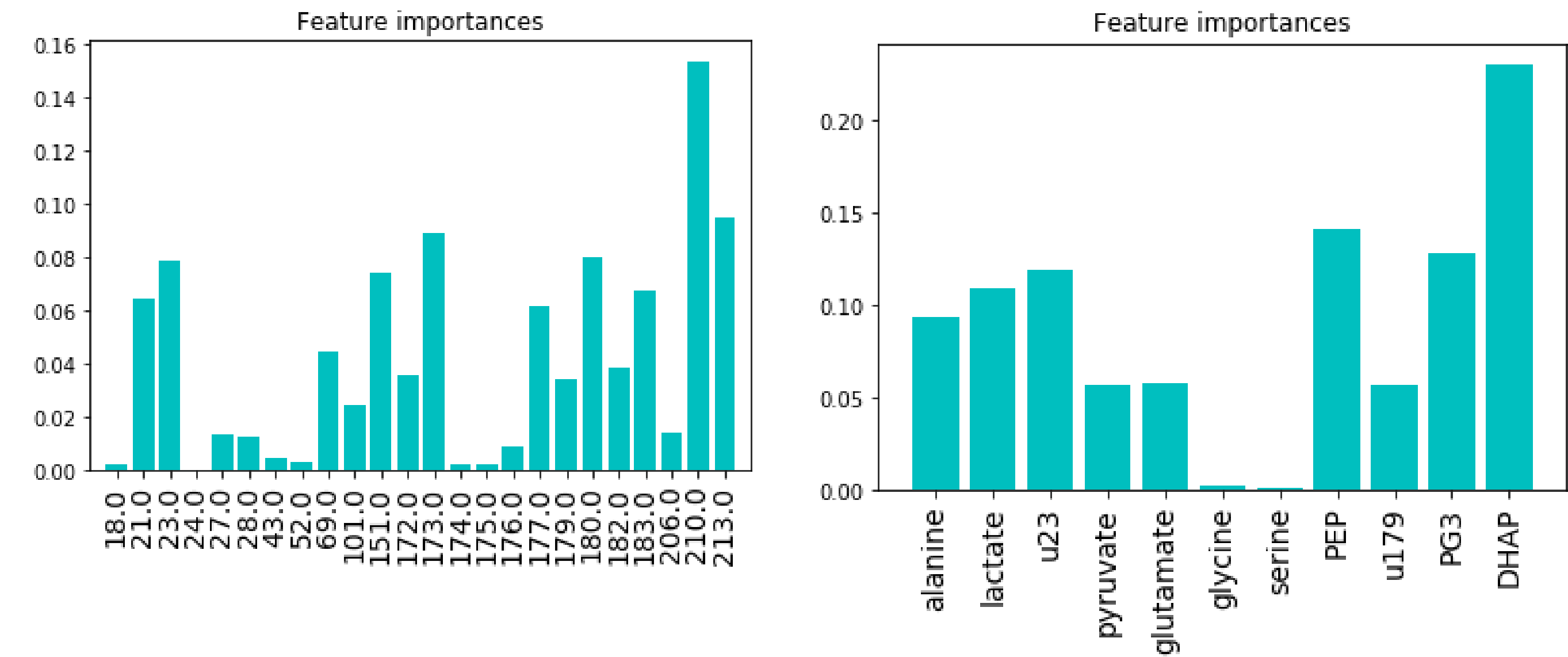


Figure 3: Graphs showing how useful each peak in the peak data (left) and each metabolite in met. data (right) is for the RF classification model.

## Biomarkers and classification

These result shows a great potential for classification of aggressiveness in prostate cancer by a PC-DFA model trained on dDNP NMR metabolomics data. RF can be used to identify biomarkers through feature extraction, and feature extraction can additionally be used for limiting the number of features used for training the PC-DFA model, possibly making a it more predictive and less likely to overfit.  
Future work could be to obtain metabolic fingerprints from prostate cells taken from biopsies on cancer patients, to investigate if the model also works on non-lab cell strains.

References:  
[1] Roberts et al. *NMR-based metabolomics: Global analysis of metabolites to address problems in prostate cancer*, (2014)  
[2] Lerche et al, *Analytical chemistry*, 1, 90 (2017)